Supplementary Information

**Fabrication of Capillary Micromechanics device**

We taper a round capillary (World Precision Inc.), of which the inner and outer diameter is 0.58 mm and 1 mm, respectively, using a micropipette puller (Sutter P-97). Subsequently, we polish the tip of the capillary to the desired diameter using sand paper. The diameter of the tip must be smaller than the diameter of the microparticle, but large enough to enable fluid to flow at large enough flow rates without an excessive pressure build-up across the device. The tip of the tapered round capillary is inserted into a water reservoir, typically made from a microcentrifugal tube. Both the tapered capillary and the water reservoir are fixed on a microscopic glass slide using epoxy glue. We then dip the untapered end of the capillary perpendicularly into a dilute suspension of microparticles. Some microparticles will be sucked into the round capillary by capillary forces. The untapered end of the round capillary is then connected to a precision pressure regulator using soft tubing (Scientific Commodities Inc.). A pressure regulator (Aignep spa, Mode. T020) is used to adjust the inlet pressure from 0 psi to 30 psi. To control the applied pressure differnce, either a high-precision pressure regulator or hydrostatic pressure can be used. By adjusting the pressure difference between the inlet and the outlet of the capillary, the flow of the microparticle suspension can be controlled to move forward or backward at different flow rates. A schematic representation of the Capillary Micromechanics set-up is shown in Figure 1.

**Mechanism of Capillary Micromechanics**

The contact area between the particle and the glass walls has the shape of a circular band; we use the pressure-dependent length $L_{\text{band}}$ and average radius $R_{\text{band}}$ of this contact band as a measure of the strain deformations in the radial direction and along the central axis of the capillary. The pressure acting on the particle from the glass wall, $p_{\text{wall}}$, is also derived from the geometry: by balancing the $z$-components of all external forces acting on the particle, one obtains

$$p_{wall} = \frac{2}{\sin(\alpha)} \frac{R_{band}}{L_{band}} p ,$$

where $\alpha$ is the tapering angle of the capillary. The characteristic stresses for a compressive and a shear deformation can then be expressed as $(2p_{wall} + p)/3$ and $(p_{wall} - p)/2$ , respectively; the corresponding characteristic volumetric and shear strains are $\Delta V/V \approx 2\epsilon_r + \epsilon_z$ and $\epsilon_r - \epsilon_z$ , respectively. In the linear elastic regime the compressive and shear modulus of the particles is then quantified by the ratio of the respective characteristic stress and the corresponding characteristic strain deformation as

$$K = \frac{\frac{1}{3}(2p_{wall} + p)}{2\varepsilon_r + \varepsilon_z} \text{, and}$$

$$G = \frac{\frac{1}{2}(p_{wall} - p)}{\varepsilon_r - \varepsilon_z} .$$

The compressive elastic modulus *K* and the shear elastic modulus *G* is thus readily evaluated by plotting the respective characteristic stress as a function of the characteristic strain deformation, where *K* and *G* correspond to the slopes of the resulting curves [25].

**Characterization of mechanical properties of single PLGA and alginate microparticles**

We first characterize the elastic properties of single PLGA and alginate microparticles using the Capillary Micromechanics technique described above; typical results are shown in Figure S1 (A-B), where we plot the characteristic stress for shear, $\sigma_{shear} = (p_{wall} - p)/2$ , and for compression, $\sigma_{comp} = (2p_{wall} + p)/3$, as a function or the respective characteristic strain deformation. Our results indicate that in the linear deformation range, alginate microparticles have an average shear and compressive modulus of *G*=9.38 ± 2.79 kPa and *K*=66.89 ± 9.19 kPa, respectively; PLGA microparticles have an average shear and compressive modulus of

$G$=91.51 ± 8.97 kPa and $K$=782.25 ± 147.8 kPa, respectively. These values are used as input parameters in the simple model description.

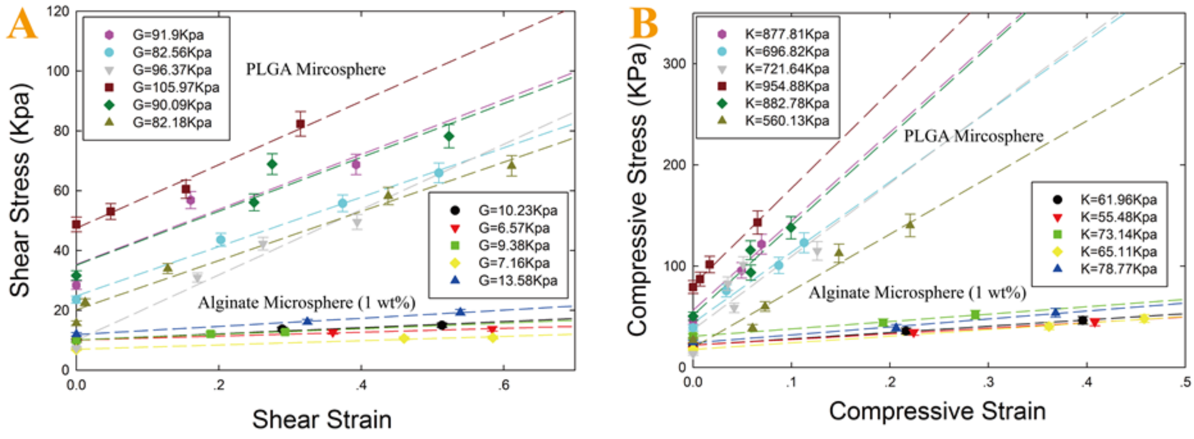


**Figure. S1.** A) & B) Compressive and shear modulus analysis for alginate and PLGA microparticles. (A) Shear elastic modulus: Plot of the characteristic shear stress $\sigma_{\text{shear}} = (p_{\text{wall}} - p)/2$ as a function of the characteristic shear strain $\epsilon_{\text{r}} - \epsilon_{\text{z}}$ ; the slope of these curves is the elastic shear modulus $G$ of the particles. (B) Compressive elastic modulus: Plot of the characteristic shear stress $\sigma_{\text{compr.}} = (2p_{\text{wall}} + p)/3$ as a function of the characteristic shear strain $2\epsilon_{\text{r}} + \epsilon_{\text{z}}$ ; the slope of these curves is the compressive modulus $K$. The error bar shows the maximum error associated with the accuracy of the applied pressure difference and the spatial precision in the digital image analysis[25] as the main sources of errors.

**Deduction of model to describe the strain stiffening behavior of core-shell microparticles with different α**

For a cylindrical inclusion of radius $R_{\text{i}}$ inside another cylinder of radius $R$, the shell strain in the radial direction can be expressed as $\varepsilon_{r,shell} = \varepsilon_r \cdot R/(R - R_i)$ , where $\varepsilon_r$ represents the macroscopic strain, based on the change in the radius of the whole cylinder. We assume that the stress within the middle section of the particle is constant; for instance, the compressive stress in the material should be matched between the core and the shell materials:

$K_{core}(2\epsilon_{r,core} + \epsilon_{z,core}) = G_{shell}(2\epsilon_{r,shell} + \epsilon_{z,shell})$

and thus the strains in the shell material will be larger than those in the core material. Assuming that the Poisson ratios of the core and shell material are independent of deformation, the longitudinal strains can be expressed as $\epsilon_{z,shell} =- 2\nu_{shell}$ and $\epsilon_{z,core} =- 2\nu_{core}$, thus enabling us to calculate the predicted ratio between the radial strains in the core and the shell material as $\beta = \frac{\epsilon_{z,core}}{\epsilon_{z,shell}} = \frac{K_{shell}(2 - 2\nu_{shell})}{K_{core}(2 - 2\nu_{core})}$; in our case, the Poisson ratios in the core and the shell material can be estimated directly from the measurements on the single component particles as $\nu = (3K - 2G)/2(3K + G)$. It turns out that for our particles the Poisson ratios of the shell and the core are similar, $\nu_{shell} = 0.43$ and $\nu_{core} = 0.443$, thus this ratio can be approximated as $\beta = K_{shell}/K_{core}$. The total radial strain applied on the particle, $\epsilon_r$ is thus a result of deformations of different extents in the shell and core materials, $\epsilon_r = \gamma\epsilon_{r,core} + (1 - \gamma)\epsilon_{r,shell}$, where $\gamma = \alpha(1 - \beta\epsilon_r)/(1 - \epsilon_r)$ is the ratio of the radii of the core and the shell, with α the radius ratio at zero deformation. As a result, the radial strain in the shell material can be expressed as a function of the overall radial strain $\epsilon_r$ as

$$\epsilon_{r,shell} = \frac{1}{1 + \beta\gamma - \gamma} = \frac{\epsilon_r}{1 - \epsilon_r - (1 - \beta)\gamma_0(1 - \beta\epsilon_r)},$$

and the radial strain in the core material given as $\epsilon_{r,core} = \beta\epsilon_{r,shell}$.

The strain deformation in the longitudinal direction is then calculated using the Poisson's ratio and the radial strain; within the middle section of the particle we then find a longitudinal strain in the shell material of

$$\varepsilon_{z,shell} =- 2\upsilon_{shell} \cdot \varepsilon_{r,shell}$$

These estimated strains now enable us to express the effective stress response in the middle section of the particle as

$$K_{middle - section} = \frac{K_{core}(2\varepsilon_{r,core} + \varepsilon_{z,core})}{2\varepsilon_r + \varepsilon_z}$$

$$G_{middle-section} = \frac{G_{core}(\varepsilon_{r,core} - \varepsilon_{z,core})}{\varepsilon_r - \varepsilon_z}$$

Further, the effective compressive $K$ and shear $G$ modulus of the whole core-shell microparticle is the sum of the modulus of the three sections weighted by their volume ratios.

$$K_{non-linear} = K_{middle-section} \cdot \left(L_{core}/L\right) + K_{shell} \cdot (1 - L_{core}/L)$$

$$G_{non-linear} = G_{middle-section} \cdot \left(L_{core}/L\right) + G_{shell} \cdot (1 - L_{core}/L)$$